09/624,946

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=> s kit#(10a) Fv (10a)(oligonucleotide# or nucleic acid#)
L1 0 KIT#(10A) FV (10A)(OLIGONUCLEOTIDE# OR NUCLEIC ACID#)

=> s Fv (p) (coupl### or attach### or bind###)(p) (oligonucleotide# or nucleic acid#)
L2 111 FV (P) (COUPL### OR ATTACH### OR BIND###)(P) (OLIGONUCLEOTIDE# OR NUCLEIC ACID#)

=> s l2 and kit#
L3 4 L2 AND KIT#

=> d l3 1-4 bib ab

L3 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2003 ACS
AN 2002:575193 CAPLUS
DN 137:139362
TI Human antibodies and fragments derived from phage display library for selective cancer therapy and diagnosis
IN Hagai, Yocheved; Lazarovits, Janette; Guy, Rachel; Lipschitz, Orly; Szanton, Esther; Levanon, Avigdor; Plaksin, Daniel; Peretz, Tuvia
PA Bio-Technology General Corp., USA
SO PCT Int. Appl., 232 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2
PATENT NO. KIND DATE APPLICATION NO. DATE

PI	WO 2002059264	A2	20020801	WO 2001-US49440	20011231
	WO 2002059264	A3	20030306		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-751181 A1 20001229

AB The present invention is directed to a peptide or polypeptide comprising an **Fv** mol., a construct thereof, a fragment of either, or a construct of a fragment having enhanced **binding** characteristics so as to **bind** selectively and/or specifically to a target cell in favor of other cells, wherein the **binding** selectivity or specificity is primarily detd. by a first hypervariable region, and wherein the **Fv** is a scFv or a dsFv, and optionally having one or more tags. The enhanced **binding** is directed to a substantially exposed and/or over-expressed **binding** site on or in a target comprising a cell in favor of other cells on or in which the **binding** site is not substantially available and/or expressed. The invention is further directed to a method for isolating such peptides and polypeptides from a phage display library and to the **nucleic acid** mols. encoding them. The invention provides for a pharmaceutical compn. comprising the peptide or polypeptide and **kits** for diagnosis and treatment of disease, specifically cancer, most specifically acute myeloid leukemia.

L3 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS

AN 2002:540186 CAPLUS

DN 137:92741

TI Oligonucleotide-attached monoclonal antibodies or fragments for immunodetection of epitopes on molecules and molecule interactions via fluorescent dyes

IN Greene, Mark I.; Zhang, Hong Tao; Li, Bin; Liu, Qindu; Murali, Ramchandran

PA USA

SO U.S. Pat. Appl. Publ., 11 pp., Cont.-in-part of U.S. Ser. No. 783,896.
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002094534	A1	20020718	US 2001-977716	20011015
	US 2002028450	A1	20020307	US 2001-783896	20010215
	WO 2002066980	A1	20020829	WO 2002-US3640	20020208

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-624946 A2 20000725
US 2001-783896 A2 20010215
US 2001-977716 A 20011015

AB Methods, systems and **kits** are provided for detecting mols. expressing a selected epitope in a sample through use of an epitope

detector contg. a single chain **Fv** for the selected epitope or a constrained epitope specific CDR, CDR mimetic or engineered CDR structure **attached** to an **oligonucleotide**. The method is useful for identifying a CDR, CDR mimetic or engineered CDR structure for use in an epitope detector or a ligand, a pharmaceutical drug or therapeutic agent.

L3 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS
AN 2002:172436 CAPLUS
DN 136:229055
TI Immuno-aRNA fluorescent detection of epitopes
IN Greene, Mark I.; Zhang, Hongtao
PA USA
SO U.S. Pat. Appl. Publ., 9 pp., Cont.-in-part of U. S. Ser. No. 624,946.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2002028450	A1	20020307	US 2001-783896	20010215
US 2002094534	A1	20020718	US 2001-977716	20011015
WO 2002066980	A1	20020829	WO 2002-US3640	20020208

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI	US 2000-624946	A2	20000725
	US 2001-783896	A2	20010215
	US 2001-977716	A	20011015

AB The authors disclose methods for detecting mols. expressing a selected epitope in a sample through use of a single chain **Fv** for the selected epitope, or a constrained epitope-specific CDR, **attached** to an dsDNA **oligonucleotide**. The dsDNA **oligonucleotide** contains the promoter for the T7 polymerase. In one example, an immobilized p185neu receptor was detected using epitope-specific scFv-**oligonucleotide** conjugate and fluorescent measurement of amplified RNA.

L3 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS
AN 2002:90343 CAPLUS
DN 136:133596
TI Sensitive detection of epitopes using antibody-based nucleic acid amplification
IN Greene, Mark I.; Eberwine, James H.; Kacharmina, Janet Estee; Zhang, Hong Tao
PA The Trustees of the University of Pennsylvania, USA
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002008757	A1	20020131	WO 2001-US22645	20010718

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,

RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
EP 1305625 A1 20030502 EP 2001-953537 20010718
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRAI US 2000-624946 A 20000725
WO 2001-US22645 W 20010718
AB The authors disclose methods and reagents for detecting mols. expressing a selected epitope in a sample through use of a "universal epitope detector". In one embodiment, the universal epitope detector is an anti-histidine tag single chain **Fv attached** to an T7 promoter-contg. double-stranded **oligonucleotide**. In an illustrative example, HER2 is captured to a solid phase using an immobilized antibody and the analyte sandwiched with a second His-tagged antibody. Addn. of the universal epitope detector and amplification of synthesized radiolabeled RNA provides for a sensitive readout and quantitation of HER2.
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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                                                         ENTRY    SESSION
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=> s complementarity determining region#(P)(coupl### or attach### or
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L1          39 COMPLEMENTARITY DETERMINING REGION#(P)(COUPL### OR ATTACH### OR
               BIND###)(10A)(OLIGONUCLEOTIDE# OR NUCLEIC ACID#)

=> s l1 and polymerase#
L2           3 L1 AND POLYMERASE#

=> s l2 and kit#
L3           0 L2 AND KIT#

=> d l2 1-3 bib ab kwic

L2   ANSWER 1 OF 3     MEDLINE
AN   2001250834     MEDLINE
DN   21244632   PubMed ID: 11320219
TI   Protein quantification from complex protein mixtures using a proteomics
     methodology with single-cell resolution.
AU   Zhang H T; Kacharmina J E; Miyashiro K; Greene M I; Eberwine J
CS   Department of Pathology, Abramson Institute for Cancer Research,
     University of Pennsylvania, Philadelphia, PA 19104-6082, USA.
SO   PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF
     AMERICA, (2001 May 8) 98 (10) 5497-502.
```

Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200106
ED Entered STN: 20010618
Last Updated on STN: 20030105
Entered Medline: 20010614
AB We have developed an extremely sensitive technique, termed immuno-detection amplified by T7 RNA **polymerase** (IDAT) that is capable of monitoring proteins, lipids, and metabolites and their modifications at the single-cell level. A double-stranded oligonucleotide containing the T7 promoter is conjugated to an antibody (Ab), and then T7 RNA **polymerase** is used to amplify RNA from the double-stranded **oligonucleotides coupled** to the Ab in the Ab-antigen complex. By using this technique, we are able to detect the p185(her2/neu) receptor from the crude lysate of T6-17 cells at 10(-13) dilution, which is 10(9)-fold more sensitive than the conventional ELISA method. Single-chain Fv fragments or **complementarity determining region** peptides of the Ab also can be substituted for the Ab in IDAT. In a modified protocol, the **oligonucleotide** has been **coupled** to an Ab against a common epitope to create a universal detector species. With the linear amplification ability of T7 RNA **polymerase**, IDAT represents a significant improvement over immuno-PCR in terms of sensitivity and has the potential to provide a robotic platform for proteomics.
AB We have developed an extremely sensitive technique, termed immuno-detection amplified by T7 RNA **polymerase** (IDAT) that is capable of monitoring proteins, lipids, and metabolites and their modifications at the single-cell level. A double-stranded oligonucleotide containing the T7 promoter is conjugated to an antibody (Ab), and then T7 RNA **polymerase** is used to amplify RNA from the double-stranded **oligonucleotides coupled** to the Ab in the Ab-antigen complex. By using this technique, we are able to detect the p185(her2/neu) receptor from. . . of T6-17 cells at 10(-13) dilution, which is 10(9)-fold more sensitive than the conventional ELISA method. Single-chain Fv fragments or **complementarity determining region** peptides of the Ab also can be substituted for the Ab in IDAT. In a modified protocol, the **oligonucleotide** has been **coupled** to an Ab against a common epitope to create a universal detector species. With the linear amplification ability of T7 RNA **polymerase**, IDAT represents a significant improvement over immuno-PCR in terms of sensitivity and has the potential to provide a robotic platform. . .

L2 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2001:301838 BIOSIS
DN PREV200100301838
TI Protein quantification from complex protein mixtures using a proteomics methodology with single-cell resolution.
AU Zhang, Hong-Tao; Kacharmina, Janet E.; Miyashiro, Kevin; Greene, Mark I. (1); Eberwine, James
CS (1) Deparments of Pathology and Laboratory Medicine, Abramson Institute for Cancer Research, University of Pennsylvania, Philadelphia, PA, 19104-6082: greene@reo.med.upenn.edu, eberwine@mscf.med.upenn.edu USA
SO Proceedings of the National Academy of Sciences of the United States of America, (May 8, 2001) Vol. 98, No. 10, pp. 5497-5502. print. ISSN: 0027-8424.
DT Article
LA English
SL English
AB We have developed an extremely sensitive technique, termed immuno-detection amplified by T7 RNA **polymerase** (IDAT) that is

capable of monitoring proteins, lipids, and metabolites and their modifications at the single-cell level. A double-stranded oligonucleotide containing the T7 promoter is conjugated to an antibody (Ab), and then T7 RNA **polymerase** is used to amplify RNA from the double-stranded **oligonucleotides coupled** to the Ab in the Ab-antigen complex. By using this technique, we are able to detect the p185her2/neu receptor from the crude lysate of T6-17 cells at 10-13 dilution, which is 109-fold more sensitive than the conventional ELISA method. Single-chain Fv fragments or **complementarity determining region** peptides of the Ab also can be substituted for the Ab in IDAT. In a modified protocol, the **oligonucleotide** has been **coupled** to an Ab against a common epitope to create a universal detector species. With the linear amplification ability of T7 RNA **polymerase**, IDAT represents a significant improvement over immuno-PCR in terms of sensitivity and has the potential to provide a robotic platform for proteomics.

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IT . . .

Systems of Organisms
cell; pyramidal neuron: nervous system

IT Diseases
cancer: neoplastic disease

IT Chemicals & Biochemicals
RNA; T7 RNA **polymerase**; antibody; double-stranded oligonucleotide: T7 promoter; p185-her2/neu receptor; peptide

IT Alternate Indexing
Neoplasms (MeSH)

IT Methods & Equipment
ELISA: analytical method; Western blot: analytical method; immuno-detection amplified by T7 RNA **polymerase**: analytical method

L2 ANSWER 3 OF 3 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

AN 2001177003 EMBASE

TI Protein quantification from complex protein mixtures using a proteomics methodology with single-cell resolution.

AU Zhang H.-T.; Kacharmina J.E.; Miyashiro K.; Greene M.I.; Eberwine J.

CS M.I. Greene, Department of Pathology, Abramson Inst. for Cancer Research, University of Pennsylvania, Philadelphia, PA 19104-6082, United States. greene@reo.med.upenn.edu

SO Proceedings of the National Academy of Sciences of the United States of America, (8 May 2001) 98/10 (5497-5502).
Refs: 36
ISSN: 0027-8424 CODEN: PNASA6

CY United States

DT Journal; Article

FS 029 Clinical Biochemistry

LA English
SL English
AB We have developed an extremely sensitive technique, termed immuno-detection amplified by T7 RNA **polymerase** (IDAT) that is capable of monitoring proteins, lipids, and metabolites and their modifications at the single-cell level. A double-stranded oligonucleotide containing the T7 promoter is conjugated to an antibody (Ab), and then T7 RNA **polymerase** is used to amplify RNA from the double-stranded **oligonucleotides coupled** to the Ab in the Ab-antigen complex. By using this technique, we are able to detect the p185(her/neu) receptor from the crude lysate of T6-17 cells at 10(-13) dilution, which is 10(9)-fold more sensitive than the conventional ELISA method. Single-chain Fv fragments or **complementarity determining region** peptides of the Ab also can be substituted for the Ab in IDAT. In a modified protocol, the **oligonucleotide** has been **coupled** to an Ab against a common epitope to create a universal detector species. With the linear amplification ability of T7 RNA **polymerase**, IDAT represents a significant improvement over immuno-PCR in terms of sensitivity and has the potential to provide a robotic platform for proteomics.
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CT Medical Descriptors:
*protein determination
analytic method
lipid analysis
promoter region
conjugation
antigen antibody complex
cell lysate
enzyme linked immunosorbent assay
human
nonhuman
rat
controlled study
human cell
animal cell
article
priority journal
*proteome
RNA polymerase
oligonucleotide
antibody
epitope
RN (RNA **polymerase**) 9014-24-8

=> dup rem l2

PROCESSING COMPLETED FOR L2
L4 1 DUP REM L2 (2 DUPLICATES REMOVED)

=> d l4 bib ab kwic

L4 ANSWER 1 OF 1 MEDLINE DUPLICATE 1
AN 2001250834 MEDLINE
DN 21244632 PubMed ID: 11320219
TI Protein quantification from complex protein mixtures using a proteomics methodology with single-cell resolution.
AU Zhang H T; Kacharmina J E; Miyashiro K; Greene M I; Eberwine J
CS Department of Pathology, Abramson Institute for Cancer Research, University of Pennsylvania, Philadelphia, PA 19104-6082, USA.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (2001 May 8) 98 (10) 5497-502.
Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200106
ED Entered STN: 20010618
Last Updated on STN: 20030105
Entered Medline: 20010614
AB We have developed an extremely sensitive technique, termed immuno-detection amplified by T7 RNA **polymerase** (IDAT) that is capable of monitoring proteins, lipids, and metabolites and their modifications at the single-cell level. A double-stranded oligonucleotide containing the T7 promoter is conjugated to an antibody (Ab), and then T7 RNA **polymerase** is used to amplify RNA from the double-stranded **oligonucleotides coupled** to the Ab in the Ab-antigen complex. By using this technique, we are able to detect the p185(her2/neu) receptor from the crude lysate of T6-17 cells at 10(-13) dilution, which is 10(9)-fold more sensitive than the conventional ELISA method. Single-chain Fv fragments or **complementarity determining region** peptides of the Ab also can be substituted for the Ab in IDAT. In a modified protocol, the **oligonucleotide** has been **coupled** to an Ab against a common epitope to create a universal detector species. With the linear amplification ability of T7 RNA **polymerase**, IDAT represents a significant improvement over immuno-PCR in terms of sensitivity and has the potential to provide a robotic platform for proteomics.
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=> dup rem l1
PROCESSING COMPLETED FOR L1

L5 15 DUP REM L1 (24 DUPLICATES REMOVED)

=> d l5 1-15 bib ab

L5 ANSWER 1 OF 15 MEDLINE DUPLICATE 1
AN 2003009407 MEDLINE
DN 22403668 PubMed ID: 12515537
TI Mutational analysis of a sequence-specific ssDNA binding lupus autoantibody.
AU Cleary Joanne; Glick Gary D
CS Department of Chemistry, University of Michigan, Ann Arbor, Michigan 48109-1055, USA.
NC GM 46831 (NIGMS)
SO BIOCHEMISTRY, (2003 Jan 14) 42 (1) 30-41.
Journal code: 0370623. ISSN: 0006-2960.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200302
ED Entered STN: 20030108
Last Updated on STN: 20030302
Entered Medline: 20030228
AB 11F8 is a murine anti-ssDNA monoclonal autoantibody isolated from a lupus prone autoimmune mouse. This mAb binds sequence specifically, and prior studies have defined the thermodynamic and kinetic basis for sequence-specific recognition of ssDNA (Ackroyd, P. C., et al. (2001) Biochemistry 40, 2911-2922; Beckingham, J. A. and Glick, G. D. (2001) Bioorg. Med. Chem. 9, 2243-2252). Here we present experiments designed to identify the residues on 11F8 that mediate sequence-specific, noncognate, and nonspecific recognition of ssDNA and their contribution to the overall binding thermodynamics. Site-directed mutagenesis of an 11F8 single-chain construct reveals that six residues within the **complementarity determining regions** of 11F8 account for ca. 80% of the binding free energy and that there is little cooperativity between these residues. Germline-encoded aromatic and hydrophobic side chains provides the basis for nonspecific recognition of single-stranded thymine nucleobases. Sequence-specific recognition is controlled by a tyrosine in the heavy chain along with a somatically mutated arginine residue. Our data show that the manner in which 11F8 achieves sequence-specific recognition more closely resembles RNA-**binding** proteins such as U1A than other types of **nucleic acid binding** proteins. In addition, comparing the primary sequence of 11F8 with clonally related antibodies that differ by less than five amino acids suggests that somatic mutations which confer sequence specificity may be a feature that distinguishes glomerulotrophic pathogenic anti-DNA from those that are benign.

L5 ANSWER 2 OF 15 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2002:344020 BIOSIS
DN PREV200200344020
TI The regulation of autoimmune anti-DNA response by idiotype-specific cytotoxic T-cells in BALB/c mice.
AU Lim, So-Yon (1); Ghosh, Swapan K. (1)
CS (1) Life Sciences, Indiana State University, 6th and Chestnut, Terre Haute, IN, 47809 USA
SO FASEB Journal, (March 20, 2002) Vol. 16, No. 4, pp. A687.
http://www.fasebj.org/. print.
Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002
ISSN: 0892-6638.
DT Conference
LA English
AB CD8+ cytotoxic T-cell (CTL) mediated control of autoreactive B-cells was

investigated using a monoclonal antibody (mAb), 2C3 (IgG1, k), derived from phthalate-immunized BALB/c mice. Since the idiotype (Ids) of 2C3 share a striking homology with those of an anti-DNA mAb, BV04-01 (IgG2b, k), from autoimmune prone (NZBxW) F1 mice, we compared its **binding** specificity for phthalate with that for autologous DNA and **oligonucleotides**. The results show that 2C3 Ig has a strong affinity both for phthalate and DNA and, in particular, for the oligonucleotides, d(pT)4 and d(pT)10. Since the Ids of 2C3 Ig express germ-line encoded Vk1 gene, it was of interest to determine if this anti-DNA response is down-regulated in non-autoimmune BALB/c mice. To assess this, six synthetic peptides based on the amino acid sequences of the Ids of 2C3 and four peptides corresponding to the Ids of non-Vk 1 related anti-DNA Ab were chosen to stimulate splenic T-cells from naive BALB/c and (NZBxW F1) mice. Among these peptides, VL1 encompassing **complementarity-determining region** 1 of 2C3 light chain induces specific CD8+ CTLs in normal BALB/c mice. VL1-peptide does not induce CTL in (NZBxW) F1 mice. CTLs from VL1-stimulated T-cells are cytotoxic to 2C3 hybridoma and VL1-peptide pulsed P815 cells, and inhibited by antibodies specific for MHC class I, beta2 microglobulin, and CD8 molecules. VL1 (Id)-specific CTLs are induced in BALB/c mice as a mechanism to counter induction of auto-reactive anti-DNA B-cells.

L5 ANSWER 3 OF 15 MEDLINE DUPLICATE 2
AN 2002055642 MEDLINE
DN 21640007 PubMed ID: 11781155
TI Systemic lupus erythematosus patients under immunosuppressive treatment express high levels of the immunoglobulin lambda variable IGLV8S1 gene with silent somatic mutations.
AU Tamia-Ferreira Marcia Cristina; Trevisan Glauce L; de Carvalho Ivan Fiore; Passos Geraldo A S
CS Grupo de Imunogenetica Molecular, Departamento de Genetica, Faculdade de Medicina de Ribeirao Preto, Universidade de Sao Paulo, Brazil.
SO BIOCHIMICA ET BIOPHYSICA ACTA, (2002 Jan 2) 1586 (1) 108-12.
Journal code: 0217513. ISSN: 0006-3002.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-AF411519; GENBANK-AF411520; GENBANK-AF411521; GENBANK-AF411522; GENBANK-AF411523
EM 200203
ED Entered STN: 20020125
Last Updated on STN: 20020308
Entered Medline: 20020307
AB Systemic lupus erythematosus (SLE) patients express high titers of somatically mutated serum autoantibodies against nuclear structures including double-stranded DNA. These somatic mutations accumulate codons for basic amino acids in the immunoglobulin variable regions of both, heavy and light chains, facilitating **binding** to **nucleic acids**. The variable (V) immunoglobulin lambda 8 (IGLV8S1) gene contributes to autoreactive B-cell repertoire of auto-immune patients. Accumulation of immune complexes of these anti-DNA autoantibodies causes severe systemic inflammation in SLE. The current treatment of lupus disease is based on immunosuppressive drugs, but the precise role for this therapy remains to be defined. To evaluate the in vivo effect of combined immunosuppressive treatment on B-lymphocytes repertoire of SLE patients, we have developed an approach using the IGLV8S1 gene as a marker. The transcription of this gene in treated SLE patients was increased. However, we observed a trend, in these patients, to conserve **complementarity determining regions** (CDRs) and framework regions (FRs) of Vlambda8 polypeptide light chain deduced sequence, from its germline counterpart. Sequencing IGLV8S1 cDNA of untreated SLE patients, taken as a control for treatment effect, displayed a decreased frequency of silent somatic mutations (consequently high

frequency of replacement mutations) in the Vlambda8 polypeptide chain deduced sequence. These data suggest that the immunosuppressive drug treatment modulates the positive selection of somatically mutated Vlambda8 light chain.

L5 ANSWER 4 OF 15 MEDLINE DUPLICATE 3
AN 2001250834 MEDLINE
DN 21244632 PubMed ID: 11320219
TI Protein quantification from complex protein mixtures using a proteomics methodology with single-cell resolution.
AU Zhang H T; Kacharmina J E; Miyashiro K; Greene M I; Eberwine J
CS Department of Pathology, Abramson Institute for Cancer Research, University of Pennsylvania, Philadelphia, PA 19104-6082, USA.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (2001 May 8) 98 (10) 5497-502.
Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200106
ED Entered STN: 20010618
Last Updated on STN: 20030105
Entered Medline: 20010614
AB We have developed an extremely sensitive technique, termed immuno-detection amplified by T7 RNA polymerase (IDAT) that is capable of monitoring proteins, lipids, and metabolites and their modifications at the single-cell level. A double-stranded oligonucleotide containing the T7 promoter is conjugated to an antibody (Ab), and then T7 RNA polymerase is used to amplify RNA from the double-stranded **oligonucleotides coupled** to the Ab in the Ab-antigen complex. By using this technique, we are able to detect the p185(her2/neu) receptor from the crude lysate of T6-17 cells at 10(-13) dilution, which is 10(9)-fold more sensitive than the conventional ELISA method. Single-chain Fv fragments or **complementarity determining region** peptides of the Ab also can be substituted for the Ab in IDAT. In a modified protocol, the **oligonucleotide** has been **coupled** to an Ab against a common epitope to create a universal detector species. With the linear amplification ability of T7 RNA polymerase, IDAT represents a significant improvement over immuno-PCR in terms of sensitivity and has the potential to provide a robotic platform for proteomics.

L5 ANSWER 5 OF 15 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 4
AN 2000:33233 BIOSIS
DN PREV200000033233
TI Thermodynamics of Fab-ssDNA interactions: Contribution of heavy chain complementarity determining region 3.
AU Komissarov, Andrey A.; Deutscher, Susan L. (1)
CS (1) Department of Biochemistry, University of Missouri School of Medicine, M121 Medical Sciences Building, Columbia, MO, 65212 USA
SO Biochemistry, (Nov. 2, 1999) Vol. 38, No. 44, pp. 14631-14637.
ISSN: 0006-2960.
DT Article
LA English
SL English
AB The recombinant anti-ssDNA Fab, DNA-1, and 16 heavy chain **complementarity determining region** 3 (HCDR3) mutant variants were selected for thermodynamic characterization of ssDNA binding. The affinity of Fab to (dT)15 under different temperatures and cation concentrations was measured by equilibrium fluorescence quenching titration. Changes in the standard Gibbs free binding energy (DELTAGdegree), enthalpy (DELTAHdegree), entropy (DELTASdegree), and the

number of ionic pairs (Z) formed upon interaction were determined. All Fab possessed an enthalpic nature of interaction with ssDNA, that was opposite to the previously reported entropically driven **binding** to dsDNA (Tanha, J., and Lee, J. S. (1997) **Nucleic Acids** Res. 25, 1442-1449). The contribution of separate residues of HCDR3 to ssDNA interaction was investigated. Analysis of the changes in DELTAHdegree and TDELTASdegree, induced by substitutions in HCDR3, revealed a complete entropy/enthalpy compensation. Mutations R98A and D108A at the ends of the HCDR3 loop produced increases in TDELTASdegree by 10.4 and 15.9 kcal/mol, respectively. Substitution of proline for arginine at the top of HCDR3 resulted in a new electrostatic contact with (dT)15. The observed linear correlation of Z and DELTAGdegree of nonelectrostatic interactions (DELTAGdegreenonel) at the anti-ssDNA combining site was used for the estimation of the specific DELTAGdegreenonel (-20 to -25 cal/(molcntdotANG2)), the average contact area (450-550 ANG2), the maximal Z (6-7), and the limit in affinity under standard cation concentrations ((0.5-1) X 108 M-1) for this family of Fab. Results suggested that rational engineering of HCDR3 could be utilized to control the affinity and likely the specificity of Ab-DNA interactions.

L5 ANSWER 6 OF 15 MEDLINE DUPLICATE 5
AN 2000016379 MEDLINE
DN 20016379 PubMed ID: 10547287
TI Fabs specific for 8-oxoguanine: control of DNA binding.
AU Bespalov I A; Bond J P; Purmal A A; Wallace S S; Melamede R J
CS Department of Microbiology and Molecular Genetics, The Markey Center for Molecular Genetics, University of Vermont, Burlington, VT 05405, USA.
SO JOURNAL OF MOLECULAR BIOLOGY, (1999 Nov 12) 293 (5) 1085-95.
Journal code: 2985088R. ISSN: 0022-2836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-AF104995; GENBANK-AF104996; GENBANK-AF104997; GENBANK-AF104998; GENBANK-AF104999; GENBANK-AF105000; GENBANK-AF105001
EM 200001
ED Entered STN: 20000124
Last Updated on STN: 20000124
Entered Medline: 20000111
AB Free radicals produce a broad spectrum of DNA base modifications including 7,8-dihydro-8-oxoguanine (8-oxoG). Since free radicals have been implicated in many pathologies and in aging, 8-oxoG has become a benchmark for factors that influence free radical production. Fab g37 is a monoclonal antibody that was isolated by phage display in an effort to create a reagent for detecting 8-oxoG in DNA. Although this antibody exhibited a high degree of specificity for the 8-oxoG base, it did not appear to recognize 8-oxoG when present in DNA. Fab g37 was modified using HCDR1 and HCDR2 segment shuffling and light chain shuffling. Fab 166 and Fab 366 which bound to 8-oxoG in single-stranded DNA were isolated. Fab 166 **binds** more selectively to single-stranded **oligonucleotides** containing 8-oxoG versus control **oligonucleotides** than does Fab 366 which **binds** DNA with reduced dependency on 8-oxoG. Numerous other clones were also isolated and characterized that contained a spectrum of specificities for 8-oxoG and for DNA. Analysis of the primary sequences of these clones and comparison with their binding properties suggested the importance of different **complementarity determining regions** and residues in determining the observed binding phenotypes. Subsequent chain shuffling experiments demonstrated that mutation of SerH53 to ArgH53 in the Fab g37 heavy chain slightly decreased the Fab's affinity for 8-oxoG but significantly improved its binding to DNA in an 8-oxoG-dependent manner. The light chain shuffling experiments also demonstrated that numerous promiscuous light chains could enhance DNA binding when paired with either the Fab g37 or Fab 166 heavy chains;

however, only the Fab 166 light chain did so in an additive manner when combined with the Fab 166 heavy chain that contains ArgH53. A three-point model for Fab 166 **binding** to **oligonucleotides** containing 8-oxoG is proposed. We describe a successful attempt to generate a desired antibody specificity, which was not present in the animal's original immune response.
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L5 ANSWER 7 OF 15 MEDLINE DUPLICATE 6
AN 1999036654 MEDLINE
DN 99036654 PubMed ID: 9819225
TI Isolation and characterization of a monoclonal anti-quadruplex DNA antibody from autoimmune "viable motheaten" mice.
AU Brown B A 2nd; Li Y; Brown J C; Hardin C C; Roberts J F; Pelsue S C; Shultz L D
CS Department of Biochemistry, North Carolina State University, Raleigh 27695, USA.
NC CA20408 (NCI)
DK07449 (NIDDK)
GM47431 (NIGMS)
SO BIOCHEMISTRY, (1998 Nov 17) 37 (46) 16325-37.
Journal code: 0370623. ISSN: 0006-2960.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199812
ED Entered STN: 19990115
Last Updated on STN: 20000303
Entered Medline: 19981217
AB A cell line that produces an autoantibody specific for DNA quadruplex structures has been isolated and cloned from a hybridoma library derived from 3-month-old nonimmunized autoimmune, immunodeficient "viable motheaten" mice. This antibody has been tested extensively in vitro and found to bind specifically to DNA quadruplex structures formed by two biologically relevant sequence motifs. Scatchard and nonlinear regression analyses using both one- and two-site models were used to derive association constants for the antibody-DNA binding reactions. In both cases, quadruplexes had higher association constants than triplex and duplex molecules. The anti-quadruplex antibody **binds** to the quadruplex formed by the promoter-region-derived **oligonucleotide** d(CGCG4GCG) (Ka = 3.3 x 10(6) M-1), and has enhanced affinity for telomere-derived quadruplexes formed by the oligonucleotides d(TG4) and d(T2G4T2G4T2G4T2G4) (Ka = 5.38 x 10(6) and 1.66 x 10(7) M-1, respectively). The antibody binds both types of quadruplexes but has preferential affinity for the parallel four-stranded structure. In vitro radioimmunofilter binding experiments demonstrated that purified anti-DNA quadruplex antibodies from anti-quadruplex antibody-producing tissue culture supernatants have at least 10-fold higher affinity for quadruplexes than for triplex and duplex DNA structures of similar base composition and length. The antibody binds intramolecular DNA triplexes formed by d(G4T3G4T3C4) and d(C4T3G4T3G4), and the duplex d(CGCGCGCGCG)2 with an affinities of 6. 76 x 10(5), 5.59 x 10(5), and 8.26 x 10(5) M-1, respectively. Competition experiments showed that melted quadruplexes are not effective competitors for antibody binding when compared to native structures, confirming that the quadruplex is bound structure-specifically. To our knowledge, this is the first immunological reagent known to specifically recognize quadruplex structures. Subsequent sequence analysis demonstrates homologies between the antibody **complementarity determining regions** and sequences from Myb family telomere binding proteins, which are hypothesized to control cell aging via telomeric DNA interactions. The presence of this antibody in the autoimmune repertoire suggests a possible linkage between autoimmunity, telomeric DNA binding proteins, and aging.

L5 ANSWER 8 OF 15 MEDLINE DUPLICATE 7
AN 1999065330 MEDLINE
DN 99065330 PubMed ID: 9850078
TI Immunity to p53 induced by an idiotypic network of anti-p53 antibodies: generation of sequence-specific anti-DNA antibodies and protection from tumor metastasis.
AU Erez-Alon N; Herkel J; Wolkowicz R; Ruiz P J; Waisman A; Rotter V; Cohen I R
CS Department of Immunology, Weizmann Institute of Science, Rehovot, Israel.
SO CANCER RESEARCH, (1998 Dec 1) 58 (23) 5447-52.
Journal code: 2984705R. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199812
ED Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981231
AB The general overexpression of p53 by different types of tumor cells suggests that p53 immunity might be generally useful for tumor immunotherapy. We describe here the induction of immunity to p53 and resistance to tumor metastasis using an idiotypic network. Mice were immunized with domain-specific anti-p53 monoclonal antibodies (Ab1): PAb-248 directed to the N-terminus; PAb-246 directed to the specific DNA-binding region; or PAb-240 directed to a mutant p53 that does not bind specific DNA. Immunized mice responded by making anti-idiotypic antibodies (Ab2) specific for the Ab1 inducer. Ab1 PAb-246 induced Ab2 that, like p53 itself, could **bind** the specific DNA **oligonucleotide** sequence of the p53 responsive element. Mice immunized with Ab1 PAb-240 or PAb-246 spontaneously made Ab3 anti-p53 antibodies that reflected the specificity of their Ab1 inducers: Ab1 PAb-246 induced Ab3 specific for wild-type p53; PAb-240 induced Ab3 specific for mutant p53. Ab1 PAb-248 induced only Ab2. The spontaneously arising Ab3 were of T cell-dependent IgG isotypes. Peptides from the **complementarity determining regions** of the Ab1 antibodies PAb-240 and PAb-246 could also induce Ab3 anti-p53. Finally, mice that produced Ab3 anti-p53 acquired resistance to tumor metastases. Therefore, an anti-idiotypic network built around certain domains of p53 seems to be programmed within the immune system, specific Ab2 antibodies can mimic the DNA binding domain of p53, and Ab3 network immunity to p53 can be associated with resistance to tumor cells.

L5 ANSWER 9 OF 15 MEDLINE DUPLICATE 8
AN 96218138 MEDLINE
DN 96218138 PubMed ID: 8647821
TI Equilibrium binding studies of recombinant anti-single-stranded DNA Fab. Role of heavy chain complementarity-determining regions.
AU Komissarov A A; Calcutt M J; Marchbank M T; Peletskaya E N; Deutsher S L
CS Department of Biochemistry, University of Missouri School of Medicine, Columbia 65212, USA.
NC GM-47979 (NIGMS)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 May 24) 271 (21) 12241-6.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199607
ED Entered STN: 19960805
Last Updated on STN: 19960805
Entered Medline: 19960722
AB We previously isolated **nucleic acid-binding**

antibody fragments (Fab) from bacteriophage display libraries representing the immunoglobulin repertoire of automimune mice to expedite the analysis of antibody-DNA recognition. In the present study, the binding properties of one such anti-DNA Fab, high affinity single-stranded (ss) DNA-binding Fab (DNA-1), were defined using equilibrium gel filtration and fluorescence titration. Results demonstrated that DNA-1 had a marked preference for oligo(dT) (100 nM dissociation constant) and required oligo(dT) >5 nucleotides in length. A detailed analysis of the involvement of the individual heavy chain (H) **complementarity-determining regions** (CDR) ensued using previously constructed HCDR transplantation mutants between DNA-1 and low affinity ssDNA-binding Fab (D5), a Fab that binds poorly to DNA (Calcutt, M. J. Komissarov, A. A., Marchbank, M. T., and Deutscher, S. L. (1996) Gene (Amst.) 168, 9-14). Circular dichroism studies indicated that the wild type and mutant Fab studied were of similar overall secondary structure and may contain similar combining site shapes. The conversion of D5 to a high affinity oligo(dT)-binding Fab occurred only in the presence of DNA-1 HCDR3. Results with site-specific mutants in HCDR1 further suggested a role of residue 33 in interaction with nucleic acid. The results of these studies are compared with previously published data on DNA-antibody recognition.

L5 ANSWER 10 OF 15 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 9
AN 1996:156003 BIOSIS
DN PREV199698728138
TI Recombinant phabs reactive with 7,8-dihydro-8-oxoguanine, a major oxidative DNA lesion.
AU Bespalov Vvan A., Andrei A. Purmal; Glackin, Mary P.; Wallace, Susan S. (1); Melamede, Robert J.
CS (1) Dep. Microbiol. Mol. Genet., Markey Cent. Mol. Genet., Univ. Vermont, Stafford Hall, Burlington, VT 05405 USA
SO Biochemistry, (1996) Vol. 35, No. 7, pp. 2067-2078.
ISSN: 0006-2960.
DT Article
LA English
AB Antibody Fabs that bind to DNA damages provide useful models for understanding DNA damage-specific protein interactions. BSA and RSA conjugates of the nucleoside and nucleotide derivatives of the oxidative DNA lesions, 7,8-dihydro-8-oxoguanine (8-oxoG) and 7,8-dihydro-8-oxoadenine (8-oxoA), were used to immunize mice. RNA from the responders was isolated and used to repertoire clone and phage display Fabs that bind to these haptens. Direct binding and competitive enzyme-linked immunosorbent assay (ELISA) demonstrated that phage Fabs (Phabs) specific for 8-oxopurine-BSA conjugates and 8-oxoguanine were produced although the Phabs did not react with 8-oxopurines in DNA. Amino acid sequence comparisons among clones having different binding properties suggested that a relatively small portion of the binding surfaces defined by the **complementarity determining regions** (CDR) accounted for hapten binding specificity, whereas other recions appeared to stabilize hapten binding by interacting with protein or DNA epitopes. Chain shuffling between 8-oxopurine-BSA binding Fabs and a DNA binding Fab showed that the heavy chain of the DNA binder conferred DNA binding capacity to the light chain of only one of the 8-oxopurine-BSA binders. Homology modeling of the 8-oxoG-specific clone g37 showed significant similarities to two previously isolated monoclonal antibodies specific for single-stranded **nucleic acids**. In the 8-oxoG Fab, which did not **bind** to DNA, the presumptive DNA binding canyon was blocked by heavy chain residues in the CDR2 region and appeared to lack part of the canyon wall due to the different placement of the light chain framework region.

L5 ANSWER 11 OF 15 MEDLINE DUPLICATE 10
AN 96186948 MEDLINE

DN 96186948 PubMed ID: 8626072
TI Analysis of a **nucleic-acid-binding** antibody fragment: Construction and characterization of heavy-chain **complementarity-determining region** switch variants.
AU Calcutt M J; Komissarov A A; Marchbank M T; Deutscher S L
CS Department of Molecular Microbiology and Immunology, University of Missouri, Columbia, 65212, USA.
NC 5R29 GM47979 (NIGMS)
SO GENE, (1996 Feb 2) 168 (1) 9-14.
Journal code: 7706761. ISSN: 0378-1119.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199606
ED Entered STN: 19960708
Last Updated on STN: 19960708
Entered Medline: 19960621
AB The display of antibody (AB) fragments (Fab) on the surface of filamentous bacteriophage (phage) and selection of phage that interact with a particular antigen (Ag) has enabled the isolation of Fab that **bind nucleic acids**. **Nucleic acid** (NA) **binding** Ab occur in vivo in connective tissue disease patients and certain inbred strains of mice and are thought to be pathogenic. Although there is ample data concerning the amino acid (aa) sequence of murine monoclonal Ab (mAb) reactive with DNA, significantly less is known about how autoAb interact with NA. The **complementarity-determining regions** (CDR) contained in the Fab contribute to most Ag binding, especially through heavy (H)-chain CDR 3. We have examined the role of individual H-chain CDR of a previously isolated recombinant single-stranded DNA-**binding** Fab (DNA-1) in **nucleic acid** interaction using a combination of H-chain CDR switching and solution-binding experiments. The three H-chain CDR of DNA-1 Fab were independently switched with the H-chain CDR of a Fab (D5) with very similar sequence and framework (FR) that binds DNA poorly in order to create all possible H-chain CDR combinations. The chimeric Fab genes were bacterially expressed, and their products were purified and analyzed. Results indicated that the H-chain CDR 3 of DNA-1 Fab, in the context of the remainder of the H-chain of D5 Fab, restored binding to oligo(dT)15 to 60% of DNA-1 levels, whereas H-chain CDR 1 and 3 of DNA-1 with CDR 2 of D5 Fab restored binding to 100% A combination of H-chain CDR 2 and 3 of DNA-1 Fab with H-chain CDR 1 of D5, unexpectedly resulted in the ability of the chimeric Fab to bind RNA preferentially over DNA. These studies demonstrate the importance of both H-chain CDR 1 and 3 in DNA recognition and further suggest that the specificity of the type of NA recognized by a particular Fab can be drastically altered by exchanging CDR.

L5 ANSWER 12 OF 15 MEDLINE DUPLICATE 11
AN 95223974 MEDLINE
DN 95223974 PubMed ID: 7708679
TI Human autoantibody recognition of DNA.
AU Barbas S M; Ditzel H J; Salonen E M; Yang W P; Silverman G J; Burton D R
CS Department of Immunology, Scripps Research Institute, La Jolla, CA 92037, USA.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1995 Mar 28) 92 (7) 2529-33.
Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 199505

ED Entered STN: 19950518
Last Updated on STN: 19970203
Entered Medline: 19950511

AB Combinatorial IgG Fab phage display libraries prepared from a systemic lupus erythematosus (SLE) donor and a healthy donor were affinity selected against human placental DNA. Human monoclonal antibody Fab fragments specific for DNA were isolated from both libraries, although Fabs of the highest affinity were isolated only from the lupus library. Generally, apparent affinities of the Fabs for human placental DNA, purified double-stranded DNA, and denatured DNA were approximately equivalent. Surface plasmon resonance indicated Fab binding constants for a double-stranded oligodeoxynucleotide of 0.2-1.3 x 10(8) M-1. The higher-affinity Fabs, as ranked by **binding** to human placental DNA or to the **oligonucleotide** probe, tested positive in the Crithidia luciliae assay commonly used in the diagnosis of SLE, and interestingly the genes encoding the heavy-chain variable regions of these antibodies displayed evidence of only minimal somatic hypermutation. The heavy chains of the SLE Fabs were characterized by a predominance of basic residues toward the N terminus of **complementarity-determining region** 3 (CDR3). The crucial role of heavy-chain CDR3 (HCDR3) in high-affinity DNA recognition was suggested by the creation of DNA binding in an unrelated antibody by HCDR3 transplantation from SLE antibodies. We propose that high-affinity DNA-binding antibodies can arise in SLE without extensive somatic hypermutation in the variable-region genes because of the expression of inappropriate HCDR3s.

L5 ANSWER 13 OF 15 MEDLINE DUPLICATE 12
AN 94148867 MEDLINE
DN 94148867 PubMed ID: 8106407
TI Sequencing and modeling of anti-DNA immunoglobulin Fv domains. Comparison with crystal structures.
AU Barry M M; Mol C D; Anderson W F; Lee J S
CS Department of Biochemistry, University of Saskatchewan, Saskatoon, Canada.
NC DK42502 (NIDDK)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1994 Feb 4) 269 (5) 3623-32.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199403
ED Entered STN: 19940330
Last Updated on STN: 19940330
Entered Medline: 19940318

AB Models for the three-dimensional structures of the combining regions of six DNA-binding antibodies have been derived from the sequence data for their Fv domains presented here. Using the amino acid sequences and the canonical structure classes described by Chothia and Lesk (Chothia, C., and Lesk, A.M. (1987) J. Mol. Biol. 196, 901), model loops were selected from immunoglobulin domains of known structure for five of the six antibody hypervariable regions. Models for the third **complementarity-determining region** of the heavy chain were constructed from known immunoglobulin loops of similar length and sequence. Comparison of three of the models with the respective crystal structure indicates that this procedure can generate a working model of the antibody combining region that provides useful information on the nature of the interactions between antibodies and nucleic acids. As part of our continuing investigation into the structural basis of antibody-DNA recognition, the observed and predicted models for the combining regions of **nucleic acid-binding** antibodies have been examined. In general, single strand-specific antibodies have deep clefts where the antigen might bind, whereas duplex-specific antibodies present a relatively flat surface. In

addition, on the basis of both sequence and structure, there is little to distinguish autoimmune antibodies from those produced by immunization. Testable hypotheses for how these antibodies might interact with single- and double-stranded nucleic acids are presented.

L5 ANSWER 14 OF 15 MEDLINE DUPLICATE 13
AN 94280777 MEDLINE
DN 94280777 PubMed ID: 8011289
TI Genetic and structural evidence for antigen selection of anti-DNA antibodies.
AU Radic M Z; Weigert M
CS Department of Microbiology and Immunology, Medical College of Pennsylvania, Philadelphia 19129.
NC CA-06927 (NCI)
GM-20964 (NIGMS)
RR-05539 (NCRR)
SO ANNUAL REVIEW OF IMMUNOLOGY, (1994) 12 487-520. Ref: 90
Journal code: 8309206. ISSN: 0732-0582.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 199407
ED Entered STN: 19940810
Last Updated on STN: 19940810
Entered Medline: 19940727
AB The primary structure of anti-DNA antibodies is highly diverse, a result of different germline variable (V) gene use, different combinations of immunoglobulin gene segments, peculiar heavy chain **complementarity determining region** 3 (H-CDR3) segments, and somatic mutations. Nevertheless, tertiary structure predictions reveal common features that yield information about likely contact sites in the anti-DNA combining site. That these contacts are involved with DNA binding is supported by recurrent features of a newly compiled set of homology groups of 13 variable regions of heavy chains (VH) and 11 variable regions of light chains (VL), characteristic pattern of somatic mutations, and the results of site-directed mutagenesis. The role of antigen in the etiology of the autoimmune response is viewed in light of recent data on overlaps between anti-DNA and anti-**nucleic acid binding** protein specificities.

L5 ANSWER 15 OF 15 MEDLINE DUPLICATE 14
AN 95085854 MEDLINE
DN 95085854 PubMed ID: 7993703
TI Autoantibodies in systemic lupus erythematosus.
AU Rahman M A; Isenberg D A
CS University College, London, United Kingdom.
SO CURRENT OPINION IN RHEUMATOLOGY, (1994 Sep) 6 (5) 468-73. Ref: 47
Journal code: 9000851. ISSN: 1040-8711.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199501
ED Entered STN: 19950126
Last Updated on STN: 19950126
Entered Medline: 19950119
AB Various autoantibodies are found in systemic lupus erythematosus. Anti-double-stranded DNA antibodies are the most pathognomonic and among the most extensively studied. Genetic studies of these antibodies and

their idiotypes suggest that high-affinity IgG anti-double-stranded DNA antibodies are produced by a process of somatic mutation and clonal expansion favoring sequences with accumulated positively charged amino acids in the **complementarity-determining regions**. The antigens that trigger this process are not known, but recent studies have suggested that a DNA-protein complex may be implicated. At the tissue level, these antibodies may react directly with membrane proteins or indirectly via complexes with DNA, histones, and heparan sulfate. Serologic studies have sought to establish links between clinical features and the presence of particular non-DNA-binding autoantibodies. Of particular interest have been antibodies to proteins with **nucleic acid-binding** potential, such as Sm, SS-A (Ro), and SS-B (La).

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=> s l1 and kit#
L6            0 L1 AND KIT#

=>
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09624.946

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L4	L3 and (epitope$1 or antibod$3 or antigen$1)	17	L4
L3	L2 and kit$1	18	L3
L2	Fv near10 (coupl$3 or attach$3 or bind$3) near10 (nucleic acid$1 or oligonucleotide$1)	28	L2
DB=DWPI,USPT,EPAB,JPAB; PLUR=YES; OP=ADJ			
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END OF SEARCH HISTORY

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Search Results - Record(s) 11 through 17 of 17 returned.

☐ 11. 5877305 . 12 Dec 94; 02 Mar 99. DNA encoding biosynthetic binding protein for cancer marker. Huston; James S., et al. 536/23.53; 424/133.1 435/328 435/69.6 530/387.3. A61K039/395.

☐ 12. 5807826 . 08 Apr 97; 15 Sep 98. Semaphorin gene family. Goodman; Corey S., et al. 514/12; 514/14 514/15 514/16 514/17 514/21. A61K038/04 A61K038/16.

☐ 13. 5723287 . 03 May 95; 03 Mar 98. Recombinant viruses displaying a nonviral polypeptide on their external surface. Russell; Stephen J., et al. 435/5; 435/235.1 435/6 536/23.4 536/23.72. C12Q001/70 C12Q001/68 C12N001/00 C07H021/04.

☐ 14. 5639856 . 13 Sep 93; 17 Jun 97. Semaphorin gene family. Goodman; Corey S., et al. 530/326; 530/327 530/328 530/329 530/330 530/350. A61K038/04 A61K038/16 C07K014/005 C07K014/435.

☐ 15. 5565331 . 12 Nov 93; 15 Oct 96. Nucleic acids encoding neural axon outgrowth modulators. Tessier-Lavigne; Marc, et al. 435/69.1; 435/320.1 435/6 536/23.5. C12N015/00 C12N015/12 C12N005/10.

☐ 16. US 20020094534 A1 WO 200266980 A1 . Detecting molecules expressing epitope, by contacting surface immobilized molecule with epitope detector, amplifying and contacting oligonucleotide bound to molecule with fluorescent dye, measuring emitted fluorescence. GREENE, M I, et al. C07H021/02 C07H021/04 C12N001/20 C12P019/34 C12Q001/68 G01N033/48 G01N033/53.

☐ 17. US 20020028450 A1 . Detecting molecules expressing a selected epitope in a sample involves using epitope detector containing single chain Fv for the selected epitope or a constrained epitope specific CDR attached to an oligonucleotide. GREENE, M I, et al. C12P019/34 C12Q001/68.

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